## Identification of DPPA4 and DPPA2 as a novel family of pluripotency-related oncogenes.

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**Public Summary:**
In order to identify novel pluripotency-related oncogenes, an expression screen for oncogenic foci-inducing genes within a retroviral human embryonic stem cell (hESC) cDNA library was conducted. From this screen, we identified not only known oncogenes but also intriguingly the key pluripotency factor, DPPA4 (developmental pluripotency-associated 4) that encodes a DNA binding SAP domain-containing protein. DPPA4 has not been previously identified as an oncogene, but is highly expressed in embryonal carcinomas, pluripotent germ cell tumors, and other cancers. DPPA4 is also mutated in some cancers. In direct transformation assays, we validated that DPPA4 is an oncogene in both mouse 3T3 cells and immortalized human dermal fibroblasts (HDFs). Overexpression of DPPA4 generates oncogenic foci (sarcoma cells) and causes anchorage-independent growth. The in vitro transformed cells also give rise to tumors in immuno-deficient mice. Furthermore, functional analyses indicate that both the DNA-binding SAP domain and the histone-binding C-terminal domain are critical for the oncogenic transformation activity of DPPA4. Down-regulation of DPPA4 in E14 mouse embryonic stem cells (mESCs) and P19 mouse embryonic carcinoma cells (mECCs) causes decreased cell proliferation in each case. In addition, DPPA4 overexpression induces cell proliferation through genes related to regulation of G1/S transition. Interestingly, we observed similar findings for family member DPPA2. Thus, we have identified a new family of pluripotency-related oncogenes consisting of DPPA2 and DPPA4. Our findings have important implications for stem cell biology and tumorigenesis. Stem Cells 2013.

**Scientific Abstract:**
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